Public Health Link

From the Chief Medical Officer for Wales

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Title: Third Primary dose of Covid-19 Vaccine for Severely Immunocompromised patients

Dear Colleagues,

Third Primary dose of Covid-19 Vaccine for Severely Immunocompromised patients

On 1 September, the Joint Committee on Vaccination and immunisation (JCVI) published a statement advising that some ***severely immunocompromised*** individuals who were immunosuppressed at the time of either their first or second primary vaccine dose should be offered a **third primary dose**.

This follows preliminary data from the OCTAVE trial, which showed that almost everyone who was immunosuppressed mounted an immune response after 2 doses of COVID-19 vaccine, as indicated by either antibodies or T cells, but in around 40% of people, the levels of antibodies were low. It is not clear to what extent this affects individuals' protection against COVID-19 as antibodies represent only part of an individual's immune response.

Most individuals whose immunosuppression commenced at least two weeks after the second dose of vaccination do ***not*** require an additional primary vaccination at this stage.
Those with less serious immunosuppression are not included in this advice but are likely to become eligible for a further dose as part of a potential booster programme, pending further advice from the JCVI.

At the current time, JCVI advises that a third dose be offered to individuals aged 12 years of age and over with severe immunosuppression in proximity of the first or second COVID-19 doses in the primary schedule. Severe immunosuppression at the time of vaccination is defined using the guidance and timings set out below:

1. Individuals with primary or acquired immunodeficiency states at the time of vaccination due to conditions including:

    - acute and chronic leukaemias, and clinically aggressive lymphomas (including Hodgkin's lymphoma) who were under treatment or within 12 months of achieving cure;

- individuals under follow up for a chronic lymphoproliferative disorders including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias (Note: this list is not exhaustive);
- immunosuppression due to HIV/AIDS with a current CD4 count of <200 cells/µl for adults Primary or acquired cellular and combined immune deficiencies – those with lymphopaenia (<1,000 lymphocytes/ul) or with a functional lymphocyte disorder;
- those who had received an allogeneic (cells from a donor) or an autologous (using their own cells) stem cell transplant in the previous 24 months;
- those who had received a stem cell transplant more than 24 months ago but had ongoing immunosuppression or graft versus host disease (GVHD); or
- persistent agammaglobulinaemia (IgG < 3g/L) due to primary immunodeficiency (e.g. common variable immunodeficiency) or secondary to disease / therapy.

2. Individuals on immunosuppressive or immunomodulating therapy at the time of vaccination including:

    - those who were receiving or had received immunosuppressive therapy for a solid organ transplant in the previous 6 months;
    - those who were receiving or had received in the previous 3 months targeted therapy for autoimmune disease, such as JAK inhibitors or biologic immune modulators including B-cell targeted therapies (including rituximab but in this case the recipient would be considered immunosuppressed for a 6 month period), T-cell co-stimulation modulators, monoclonal tumour necrosis factor inhibitors (TNFi), soluble TNF receptors, interleukin (IL)-6 receptor inhibitors., IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors. (N.B: this list is not exhaustive); or
    - those who were receiving or had received in the previous 6 months immunosuppressive chemotherapy or radiotherapy for any indication.

3. Individuals with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to vaccination including:

    - high dose corticosteroids (equivalent ≥ 20mg prednisolone per day) for more than 10 days in the previous month;
    - long term moderate dose corticosteroids (equivalent to ≥10mg prednisolone per day for more than 4 weeks) in the previous 3 months;
    - non-biological oral immune modulating drugs e.g. methotrexate >20mg per week (oral and subcutaneous), azathioprine >3.0mg/kg/day; 6-mercaptopurine >1.5mg/kg/day, mycophenolate >1g/day) in the previous 3 months; or
    - certain combination therapies at individual doses lower than above, including those on ≥7.5mg prednisolone per day in combination with other immunosuppressants (other than hydroxychloroquine or sulfasalazine) and those receiving methotrexate (any dose) with leflunomide in the previous 3 months

4. Individuals who had received high dose steroids (equivalent to >40mg prednisolone per day for more than a week) for any reason in the month before vaccination

Individuals who had received brief immunosuppression (≤40mg prednisolone per day) for an acute episode (e.g. asthma / COPD / COVID-19) and individuals on replacement corticosteroids for adrenal insufficiency are not considered severely immunosuppressed sufficient to have prevented response to the primary vaccination.

As per current advice in Chapter 14a of the Green Book, the JCVI has advised that “individuals who have received a bone marrow transplant after vaccination should be considered for a re-immunisation programme for all routine vaccinations and for COVID-19”. Re-vaccination with a 2-dose schedule should be considered 3-6 months post autologous and allogeneic human stem cell transplant or CAR-T therapy. A third dose of vaccine should be administered, at least 8 weeks after the second dose (in line with the advice above).

JCVI advises a preference for mRNA vaccines (i.e. Pfizer or Moderna vaccine) for the third primary dose, with the option of the AstraZeneca Vaxzevria vaccine for individuals who have received this vaccine previously where this would facilitate delivery. At this stage for supply reasons, we do not expect AstraZeneca Vaxzevria to be routinely used for third primary doses.

The decision on the timing of the third dose should be undertaken with the specialist involved in the care of the patient especially where timing is key. In general, vaccines administered during periods of minimum immunosuppression (wherever possible) are more likely to generate better immune responses. The third dose should be given at least 8 weeks after the second dose, with special attention paid to current or planned immunosuppressive therapies. Where possible the third dose should be delayed until two weeks after the period of immunosuppression, in addition to the time period for clearance of the therapeutic agent. If not possible, consideration should be given to vaccination during a treatment ‘holiday’ or at the lowest point of immunosuppression between doses of treatment.

At this time, provision of a third primary dose to persons who are immunosuppressed is based on the premise there are unlikely to be significant harms or disadvantages whilst offering possible benefit. Uncertainties in respect of individual harms and benefits will need to be communicated as part of informed consent, and expectations regarding the value of a third primary dose taken into account.

Booster Doses

In the event of a booster programme, it is expected that severely immunosuppressed people will also be offered a booster dose, at a suitable interval after their third dose.

Operational aspects

Health board vaccination leads are working with Digital Health and Care Wales, Public Health Wales and the Welsh Government through the central COVID-19 Vaccination Programme team, to facilitate local deployment of this guidance, which we appreciate is complex.

Pharmaceutical advice both locally and centrally will be available to support identification of eligible individuals from dispensing data.

Organisational support for health board vaccination teams to enable vaccination of these persons within the optimal timing window for them, should be considered a priority.

Medical Directors and Associate Medical Directors are requested to cascade this through relevant specialist clinical teams. Further advice will follow through Health Board COVID-19 vaccine leads. This is a complex task and identification of relevant patients will be supported by DHCW, alongside Clinicians own systems.

Updates to the Green Book, PGDs, public and health care information are being developed and will be available here:
http://nww.immunisation.wales.nhs.uk/covid-19-vaccination-programme

For further information the relevant local links are outlined below, where queries can be passed to the relevant lead;

BCU.SROCovid19VaccinationProgramme@wales.nhs.uk
Cvuhb.massimms@wales.nhs.uk
Powys.covidvacc@wales.nhs.uk
covidenquiries.hdd@wales.nhs.uk
ABB.CV19TeamLeaders@wales.nhs.uk
CTM_ImmunisationService@wales.nhs.uk
sbu.covidbookingteam@wales.nhs.uk

Attachments

1. JCVI Press Notice - Written Statement: COVID-19 Vaccination - JCVI advice offering further vaccinations to individuals who are severely immunosuppressed (2 September 2021) | GOV.WALES
2. FAQs – Uploaded separately

Yours sincerely

DR FRANK ATHERTON
Chief Medical Officer

Dr Gillian Richardson
Deputy Chief Medical Officer (Vaccines)

Appendix 1

To: Health Boards and NHS Trusts:

Chief Executives

Medical Directors

Nurse Directors

Hospital Principals and Chief Pharmacists

To: NHS Wales Shared Services Partnership to cascade to:

- GPs
- Community Pharmacists
- Independent hospitals

Cc: Public Health Wales
Directors of Public Health